Assessment of pulmonary function of preterm newborn infants with respiratory distress syndrome at different positive end expiratory pressure levels

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Abstract

Objective: to verify the alterations of pulmonary function in preterm newborn infants with respiratory distress syndrome (RDS). The parameters analyzed were Dynamic Compliance (Cdyn), Inspiratory Tidal Volume (TVinsp), partial arterial pressure of carbon dioxide (PaCO2).

Methods: eleven preterm newborn infants, with gestational age < 35 weeks, and birth weight < 2,500 g, were included in a control case study. All infants presented RDS and were treated with 120 mg/Kg of porcine surfactant. The initial positive end expiratory pressure (PEEP) was 3 cm H2O. A pneumotachograph with a graphical monitor was used to assess the pulmonary function. After each increase in the PEEP (4 and 6 cm H2O), there was an interval of 20 minutes before measuring the arterial data of pulmonary function and arterial gases.

Results: there were three males and eight females (1:2.7) among the infants with RDS. The mean gestational age was 30.78 ± 2.05 weeks, ranging from 26 to 34 weeks. The increase in the PEEP from 3 to 6 cm H2O caused a significant decrease in the TVinsp (6.46 ± 3.43 to 4.20 ± 2.35, p=0.0262). With the increase in the PEEP from 4 to 6 cm H2O, there was also a decrease in the TVinsp (5.98 ± 3.33 to 4.20 ± 2.35), (p=0.0044). Regarding the Cdyn, when there was an increase in the PEEP from 3 to 6 cm H2O, the reduction was statistically significant (0.58 ± 0.27 to 0.46 ± 0.25, p=0.0408) and from 4 to 6 cm H2O, the reduction in the Cdyn was also important (0.77 ± 0.27 to 0.46 ± 0.25, (p=0.0164). Increases in the PEEP from 4 to 6 cm H2O caused increases in the PaCO2 (52.81 ± 15.49 to 64.90 ± 12.69), (p=0.0141). A more significant increase was observed when the PEEP was elevated from 3 to 6 cm H2O (41.45 ± 7.87 to 64.90 ± 12.69, p=0.0033).

Conclusions: the study showed that the PEEP from 3 to 4 cm H2O produces better results in terms of Cdyn and less collateral effects regarding respiratory acidosis and pulmonary hyperventilation with impairment of the alveolar ventilation, evidenced by the increase in the PaCO2 and the decrease in the TVinsp.

Introduction

The respiratory distress syndrome (RDS), more than a disease process, is a developmental disorder that is generally associated with premature birth. Despite great advances in understanding the pathophysiology of RDS and the role surfactant plays as a cause, it remains the principal clinical problem and one of the most common causes of morbidity in preterm newborns (PTNs). Of all the respiratory problems that affect newborns, hyaline membrane disease is one of the most serious and frequent. Close to 50% of deaths that occur in the neonatal period are related to respiratory disorders. RDS is present in approximately 80 to 90% of the cases, during the first week of life.

Nearly 30% of PTNs with RDS generally require the use of continuous distension pressure, whether as continuous positive airway pressure (CPAP), or through tracheal intubation with positive end expiratory pressure (PEEP). In the treatment of PTNs with hyaline membrane disease, principally those who are submitted to mechanical ventilation, respiratory mechanics should be intensely monitored. Flow and volume analysis, through pneumotachograph, is widely used. Pressure-volume curves are also determined by this equipment. Dynamic compliance, inspiratory and expiratory tidal volume and system air loss can be continuously and simultaneously evaluated. Therefore, it is possible to minimize the adverse effects of mechanical ventilation, from the use of PEEP, and thus prevent lung injury (barotrauma and volutrauma), cardiocirculatory and systemic injuries.

The object of the present study is to evaluate alterations to lung function: Dynamic compliance (CDyn), inspiratory tidal volume (VTinsp), and alterations to arterial carbon dioxide pressure (PaCO₂), in preterm newborns with respiratory distress syndrome with PEEP of 3.4 to 6 cm H₂O.

Patients and Methods

Eleven PTNs with gestational age less than 35 weeks and with birthweight less than 2,500 grams were evaluated by modified Ballard method. Both clinical and radiological diagnosis of RDS was established in all PTNs. All patients were admitted to the NICU of the Teaching Hospital of Universidade Federal de Mato Grosso do Sul (HU - UFMS). They were under mechanical ventilation and were submitted to the study after presenting clinical data and stable blood gases for at least two hours after surfactant administration. Permission and a signed consent form was obtained from the parents for the participation of their children in the study. The research was approved by the Medical Ethics Committee of UFMS.

All the newborns were sedated and curarized, if necessary, so that spontaneous respiration and/or breathing effort would not interfere with the assessment of lung function. Children with cardiac, pulmonary, neuromuscular or renal diseases, malformations, and hydroelectric, metabolic or cardiocirculatory disorders were not included in the study.

The clinical diagnosis was based on the criteria adopted by Walter and Taeusch, which include clinical and radiological data.

Soon after the diagnosis of RDS, the patients received porcine surfactant (Curosurf®) in the dose of 120 mg/kg (1.5 ml is equivalent to 120 mg). Depending on the clinical development and on the results of the blood gas analysis, the patients received a second dose.

The umbilical artery was properly catheterized. Blood gases were measured from a sample of blood heparinized (50 units) in an insulin syringe. The analyses were performed with a Radiometer ABL 330 for different PEEP levels (3 cm H₂O, 4 cm H₂O and 6 cm H₂O) at an interval of twenty minutes between them. Pulse oximetry was carried out continuously, from the arrival of the patient up to the end of the blood gas analysis, by means of a digital Ohmeda oximeter. A pulse oximeter transducer was placed at the level of the right thumb.

A time-cycled, pressure-limited ventilator - Sechrist IV 100B (Sechrist, Anaheim, California, USA) - was used. The initial ventilatory parameters (PIP, RF, IT, ET, I/E ratio and FiO₂) were adjusted with the objective of maintaining blood gases at predetermined levels: pH between 7.20 and 7.40; PaCO₂ between 20 and 50 mmHg; PaO₂ between 50 and 80 mmHg and Hb saturation ≥90%. The initial PEEP was 3 cm H₂O.

After the patient remained stable for at least two hours after surfactant administration, PEEP levels were changed from 4 to 6 cm H₂O. Twenty minutes were allowed for a new blood gas analysis between one PEEP increase and the other.

To guarantee saturation above 90%, the remaining ventilator parameters, except for FiO₂, were not altered in order to eliminate confounding variables. Each PEEP level was maintained for 20 minutes and, at the end of this period, blood gases (PaCO₂ and PaO₂) were analyzed.

A pneumotachograph with a graphic monitor, Newport Navigator GM - 250, (NMI Newport Medical Instruments, INC, USA), coupled with a Varley - Bicore flow transducer was used to evaluate lung function. Air was not allowed to escape through the lateral walls of the tube, as evaluated by the same pneumotachograph (the pneumotachograph detected whether the air escaped). The following parameters were measured for each PEEP level after twenty minutes with the aim of stabilizing the patient: dynamic compliance (CDyn), in milliliters/centimeters of H₂O; inspiratory tidal volume (VTinsp), in liters.

The mean, standard deviation and percentage were calculated for statistical analysis of the results. The Shapiro-Wilk test was used to verify the normality of the variables. The Wilcoxon signed-rank test (Wilcoxon apud Daniel, 1995) was used to compare the differences between groups.
before and after PEEP increases. The p value was considered significant if less than 0.05. All statistical tests were performed using Microsoft® Excel 4.0, licensed by the Center for Pediatric Improvement (CAPE), of the Pediatric Department of UFMS, under the identification number 61616, and the program Stataquest 4.0 for Windows 95, serial number: W-902103040, Stata Corporation TX, USA.

Results

Of the 11 patients with RDS, three were male and eight were female (1:2.7). Gestational age was 30.78± 2.05 weeks, with a variation of 26 to 34 weeks. Birthweight ranged from 860 to 2,270 grams, with a mean and standard deviation of 1,489.10 ± 358.28 grams, respectively. The average time for the administration of the first dose of exogenous surfactant was 7.5± 6.54 hours, with a variation of 1.5 to 24 hours.

For the PEEP levels of 3.4 and 6 cm H$_2$O, the values corresponding to dynamic compliance (CDyn), inspiratory tidal volume (VTinsp); and arterial carbon dioxide pressure (PaCO$_2$) are shown in Table 1.

With a PEEP increase of 3 to 4 cm H$_2$O, there was a reduction in the VTinsp from 6.46± 3.43 to 5.98± 3.33, respectively. However, this difference was not statistically significant (p=0.4234). The PEEP increase from 3 to 6 cm H$_2$O immediately caused a statistically significant reduction in VTinsp (from 6.46± 3.43 to 4.20±2.35, p=0.0262). With the PEEP increase from 4 to 6 cm H$_2$O, there was also a statistically significant reduction in VTinsp (from 5.98± 3.33 to 4.20± 2.35, p=0.0044).

In terms of dynamic compliance, the effects of the PEEP increase from 3 to 4 cm H$_2$O, showed no statistically significant alterations (p=0.5045). When the PEEP increase was from 3 to 6 cm H$_2$O, the CDyn decrease was statistically significant (0.58± 0.27 to 0.46± 0.25, p=0.0408) and from 4 to 6 cm of H$_2$O the CDyn decrease was also important (0.77± 0.27 to 0.46± 0.25, p=0.0164).

Positive end expiratory pressure increases from 3 to 4 cm H$_2$O did not alter PaCO$_2$ (41.45± 7.87 to 52.81± 15.49, p=0.0749). H$_2$O increases of 4 to 6 cm caused statistically significant increases in PaCO$_2$ (52.81± 15.49 to 64.90±12.69, p=0.0141). A more pronounced increase was observed when PEEP was altered from 3 to 6 cm H$_2$O (41.45± 7.87 to 64.90±12.69, p=0.0033).

Table 1 - Values of pulmonary function parameters and PaCO$_2$, obtained with PEEP of 3, 4 and 6 cm H$_2$O, from newborns with RDS

<table>
<thead>
<tr>
<th>Patients</th>
<th>CDyn*</th>
<th>VTinsp †</th>
<th>PaCO$_2$ ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PEEP3</td>
<td>PEEP4</td>
<td>PEEP6</td>
</tr>
<tr>
<td>1</td>
<td>0.31</td>
<td>0.28</td>
<td>0.18</td>
</tr>
<tr>
<td>2</td>
<td>0.87</td>
<td>0.78</td>
<td>0.55</td>
</tr>
<tr>
<td>3</td>
<td>0.24</td>
<td>0.34</td>
<td>0.39</td>
</tr>
<tr>
<td>4</td>
<td>1.1</td>
<td>1.27</td>
<td>0.80</td>
</tr>
<tr>
<td>5</td>
<td>0.92</td>
<td>1.02</td>
<td>1.04</td>
</tr>
<tr>
<td>6</td>
<td>0.56</td>
<td>0.62</td>
<td>0.45</td>
</tr>
<tr>
<td>7</td>
<td>0.39</td>
<td>0.29</td>
<td>0.25</td>
</tr>
<tr>
<td>8</td>
<td>0.63</td>
<td>0.63</td>
<td>0.42</td>
</tr>
<tr>
<td>9</td>
<td>0.44</td>
<td>0.30</td>
<td>0.33</td>
</tr>
<tr>
<td>10</td>
<td>0.58</td>
<td>0.56</td>
<td>0.4</td>
</tr>
<tr>
<td>11</td>
<td>0.41</td>
<td>0.33</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Mean and SD: 0.58± 0.77± 0.46± 6.46± 5.98± 4.20± 41.45± 52.81± 64.90±

* dynamic compliance; † inspiratory tidal volume; ‡ arterial carbon dioxide pressure.

PEEP from 3 to 6 cm H$_2$O, decrease in VTinsp (p=0.0262). PEEP from 4 to 6 cm H$_2$O, decrease in VTinsp (5.98± 3.33 to 4.20±2.35, p=0.0044).

PEEP 3 to 6 cm H$_2$O, decrease in CDyn (p=0.0408); PEEP 4 to 6 cm H$_2$O, decrease in CDyn, (p=0.0164).

PEEP 4 to 6 cm H$_2$O, increase in PaCO$_2$ (p=0.0141); PEEP from 3 to 6 cm H$_2$O (p=0.0033).
Discussion

In mechanical ventilation of preterm newborns with RDS, even with surfactant administration, PEEP is largely used to prevent alveolar collapse, maintain functional residual capacity (FRC) and improve oxygenation. PEEP refers to the maintenance of positive airway pressure during expiration, combined with intermittent mechanical ventilation with positive pressure. This results in a better distribution of ventilation in regions with a low V/Q (ventilation perfusion) of the lungs, and in a better V/Q balance. Therefore, PEEP has a paramount importance to the improvement of oxygenation, the decrease in the necessity for high concentrations of inhaled O2, increase of FRC and improvement of total respiratory compliance in the cases of diseases associated with low residual volume and compliance.

Falke et al. (1972) studied ten mechanically-ventilated newborns with acute respiratory insufficiency and verified the effect of PEEP of 0, 10 and 15 cm H2O applied every 30 minutes. CDyn progressively decreased as PEEP was increased (p<0.01) and PaO2 increased when PEEP was altered from 5 to 15 cm H2O (p<0.01). The reduction in CDyn results in the enhanced stiffness of highly distended alveoli. On the other hand, the rise in PaO2 could indicate simultaneous recruitment of air spaces associated with the hyperinflation of previously open alveoli. Philips III et al. (1980) evaluated CDyn in twenty-four preterm newborns with RDS, associated with PEEP, and observed significant reductions (p<0.05) for each PEEP increase. In the present study, the effects of PEEP increase from 3 to 4 cm H2O did not cause significant alteration to CDyn (p=0.5045). With a PEEP increase from 3 to 6 cm H2O, there was a statistically significant decrease in CDyn (p=0.0408), as occurred with PEEP from 4 to 6 cm H2O (p=0.0164).

The reduction in CDyn could be explained by the fact that the application of a PEEP greater than 3 or 4 cm H2O could lead to alveolar expansion and to an increase in FRC. Alveoli that are more expanded have a greater elastic recoil pressure, and since they share a common airway, some air tends to follow the pressure gradient and moves to other alveoli. Presumably, this limit represents the point at which the maximum recruitment of air space was reached. Additional PEEP increases will merely overexpand the the open air spaces. CDyn is reduced from this moment on.

Dimitrou et al. (1999) studied eight premature newborns and found average CDyn values for three PEEP levels. Field et al. (1985) evaluated 15 patients with RDS and observed CDyn variations related to the PEEP variations. When the results of this study are compared with literature data, only the PEEP of 6 cm H2O are similar to the findings of Dimitrou et al. (1999) In comparison with the data obtained by Graff (1986), the values are very similar, especially regarding PEEP levels of 3 and 4 cm H2O and the levels obtained by Field et al. (1985).

The data obtained in this study show that the best CDyn average was that produced by a PEEP of 4 cm H2O (0.77±0.62). According to Cheifetz et al. (1998), a reduction greater than or equal to 20% in CDyn indicates the presence of lung hyperinflation. The greatest CDyn reductions occurred between a PEEP increase from 3 to 6 cm H2O (21.42%) and a PEEP increase from 4 to 6 cm H2O (40.25%), which explain the other alterations caused by probable lung hyperinflation.

It is therefore clear that an adequate PEEP prevents alveolar collapse and maintains the volume at the end of expiration, thus improving the V/Q ratio, and increasing PaO2. Since PEEP variations modify the pressure gradient between inspiration and expiration, carbon dioxide (CO2) elimination can be affected. This way, an elevation in PEEP can diminish tidal volume and CO2 elimination, leading to a rise in partial arterial carbon dioxide pressure (PaCO2). Therefore, alveolar hypoventilation should occur after PEEP increase, followed by a corresponding increase in PaCO2. Thus, a PEEP reduction should be considered when CO2 retention occurs, especially if hypoxemia is not a problem.

In the present study, a PEEP increase from 3 to 4 cm H2O did not lead to significant alterations in PaCO2 (41.45±7.87 to 52.81±15.49, p=0.0749). Increases from 4 to 6 cm H2O caused a statistically significant increase in PaCO2 (52.81±15.49 to 68.90±12.69, p=0.0141). A more pronounced increase was observed when PEEP was increased from 3 to 6 cm H2O (41.45±7.87 to 64.90±12.69, p=0.0033).

Another consequence of tidal volume reduction and, consequently of alveolar ventilation, is CO2 retention and probable respiratory acidosis. It has been shown that after PEEP increases from zero to 6 cm H2O, there was average reduction in pH of 7.33 (7.3-7.43) with PEEP of 3 cm H2O and an average of 7.29 (7.16 to 7.38) for PEEP of 6 cm H2O.

Likewise, Bartolomew et al. (1999) observed that a reduction in tidal volume (VT) diminished the minute volume and also had implications on CO2 exchange. A reduction in PEEP of 2 cm H2O increased the tidal volume by 30%. This effect is determined by ventilation/minute in accordance with the alveolar air equation: PaCO2 = VT/minute volume + K, where K is a constant. VCO2 is the volume of CO2 produced. This is especially applied to extremely premature newborns in whom alveolar ventilation may already be compromised by an anatomically disproportionately large space. The ratio of dead space volume and VT is an important determinant of alveolar ventilation and can be significantly improved by a VT increase or diminished by VT reduction.

Philips III et al. (1980) also concluded that if the tidal volume falls due to a PEEP increase, the minute volume also falls; therefore, increased alveolar expansion and intrathoracic pressure lead to CO2 retention, alveolar collapse and/or a decrease in cardiac output.
In this study, with a PEEP increase from 3 to 6 and from 4 to 6 cm H₂O, VTinsp diminished significantly (p=0.0262 and p=0.0044, respectively).

The study thus evidenced that PEEP of 3 and 4 cm H₂O produces better results in terms of CDyn and fewer adverse effects in terms of respiratory acidosis and lung hyperinflation, with a decrease in alveolar ventilation, characterized by an increase in PaCO₂ and a decrease in VTinsp.

References


